REMARKS

A. Regarding the Amendments

Claims 13-16 and 23 have been amended as set forth in the above complete listing of the claims. As amended, the claims are supported by the specification and the original claims. Thus, upon entry of the amendments, claims 10, 11 and 13-23 will be pending.

B. Response to Restriction/Election Requirement

Applicants acknowledge the Examiner's further restriction of new claims 24-43 and elect claims 10-11 and 13-23, with traverse. Non-elected claims 1-9, 12 and 24-43 are acknowledged above, in the listing of the claims, as withdrawn. Applicants respectfully reserve the right to pursue these claims in a related application, without prejudice.

C. Priority Request

The Examiner has alleged that Applicants have not complied with the requirements for receiving the benefit of an earlier filing date under 35 U.S.C. §120. Applicants respectfully submit that the request for priority was submitted with the filing of the application on July 20, 2001. However, the priority information had not been added to the specification. By the present amendment, entry of Applicants' priority claim into the text of the specification is respectfully requested. Priority of the invention is claimed to U.S. Application No. 09/042,428, filed March 13, 1998, now issued U.S. Patent No. 6,294,355, and to U.S. Provisional Application No. 60/036,553, filed March 14, 1997. Incorporation by reference of both of these applications is respectfully requested by the present amendment.

D. Objection to the Specification or Claims

Claim 13 was objected to as allegedly lacking reference to the appropriate SEQ ID NOs. The Examiner's attention is respectfully drawn to claim 13 as set forth above and currently

amended. Claim 13 now contains the sequence identifiers 10 and 11, to identify the 4 amino acid sequences set forth therein. These sequence identifiers were identified as such in the Sequence Listing submitted on February 21, 2002. Similarly, the specification has also been amended, to insert sequence identifiers, where necessary. Entry of these amendments is respectfully requested. As the amendments to the claims render the objection moot, withdrawal of the objection is respectfully requested.

Claim 23 is objected to as containing the unclear term "125I." Amendment of the claim has been requested by the present action, such that the term has been amended to "^{125}I." The claim, as amended is set forth above in the complete listing of the claims. As such, the Examiner's objection is rendered moot and withdrawal is respectfully requested.

E. Rejection Under 35 U.S.C. § 112

Applicants respectfully traverse the rejection of claims 10-11 and 13-23 under 35 U.S.C. § 112, first paragraph, for containing subject matter allegedly not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the invention at the time of filing of the Application. In particular, it is alleged in Paper No. 12 that claims 10-11, 16, 18, 19 and 20-23 are not supported in the specification, as indicated upon their submission. Applicants respectfully disagree.

Claim 10, as amended in the preliminary amendment submitted on February 27, 2003, is rejected as allegedly having removed the limitations to the "isolated components." Applicants do not understand this rejection and clarification is requested. By the amendment mailed February 27, 2003, claim 10 was amended to correct misspelling of the word "binding," to change the term "said" to "the" throughout the claim and to substitute "substantial sequence identity" with the more detailed "at least 70% sequence identity." In the amended claim, and in the claim as it stands upon entry of this amendment, both the synaptic activation protein of part (i) and the binding protein of part (ii) are set forth as isolated. Therefore, it is respectfully submitted that the

subject matter of claim 10 does recite use of an isolated synaptic activation protein and an isolated binding protein. Clarification or withdrawal of the Examiner's rejection is respectfully requested.

Claim 11 as amended in the preliminary amendment submitted on February 27, 2003, is rejected as allegedly not supported in the specification. Applicants respectfully disagree. The Examiner has alleged that there is no support in the specification for an mGluR other than one that contains an SSSL or SSTL sequence. The Examiner's attention is respectfully drawn to the specification, for example, at page 4, lines 3-7, where clarification of the binding protein is set forth. Various exemplary embodiments are set forth where the binding protein is: 1) a mGluR containing an SSSL or SSTL sequence; 2) a mGluR linked to PI-PLC; and 3) mGluR that is expressed in cells. It is respectfully submitted that these embodiments are set forth as exemplary and are not meant to be exclusionary. Other binding proteins, including other mGluRs are therefore possible and would have been known to one of skill in the art. Guidance for determining these other mGluRs is provided in the specification, for example, at page 17, lines 11-13, where it is stated that "[s]pecific binding sites [other than SSSL and SSTL] for other synaptic activation proteins may have similar or divergent amino acid sequences that can be empirically determined, using methods similar to those discussed above." Accordingly, it is respectfully submitted that one of skill in the art would have known that the methods of the invention encompassed mGluRs other than those containing SSSL or SSTL C-terminal sequences. Withdrawal of the rejection of claim 11 as allegedly not having a basis in the specifcation is respectfully requested.

Claim 16, as submitted in the preliminary amendment submitted on February 27, 2003, was stated as supported on page 18. The Examiner's attention is respectfully drawn to page 18, line 20-21, where it is stated that "[f]or example, purified synaptic activation protein can be coated onto a solid phase..." In accordance with the Examiner's rejection, the language in the claim has been amended to mirror the language in the specification. Therefore, the language of

the claim is fully supported by the language at page 18, line 20-21. Withdrawal of the Examiner's rejection of claim 16 is therefore respectfully submitted.

Claim 18 recites that the means for detecting binding is a GST pulldown. The Examiner alleges that because this terminology is not specifically set forth in the specification or Examples, that this terminology is not supported by the specification. Applicants respectfully disagree. It is respectfully submitted that the term "pulldown" is known in the art as an assay that can isolate protein complexes by using affinity tags that are present in a protein within the complex. Therefore a pulldown utilizing GST as a tag would be known as a GST pulldown. The Examiner's attention is respectfully drawn to Example 7. In Example 7, a GST-Homer fusion protein is run through a Homer affinity column, where the GST-Homer fusion protein is irreversibly crosslinked to agarose beads. The bound mGluR5 was then obtained by lysing and elution. It is respectfully submitted that one of skill in the art would recognize this assay as a GST pulldown. Accordingly, the use of such terminology in the claims is supported by the specification and withdrawal of the rejection is respectfully submitted.

Regarding claims 18 and 19, it is alleged that the detection methods of those claims are not disclosed in examples 6 and 7 with respect to methods of selecting a protein that interferes with binding of a synaptic activation protein. Applicants respectfully disagree. Examples 6 and 7 are not meant to be limiting to the application, but are merely set forth as exemplary methods of the detection step of the invention. Example 7, in particular, discloses methods of detecting binding of mGluR5 to the Homer protein. If a test compound does interfere with the binding of the mGluR5 to the Homer protein, the GST pulldown or coimmunoprecipitation will detect that the binding in the presence of the test compound is different than the binding not in the presence of the test compound. Accordingly, the compound may be identified as a compound that interferes with the binding of a synaptic activation protein (for example, Homer) with a cellular binding protein (for example, mGluR5). The Examiner's attention is also respectfully drawn to part B of Example 9, which cites an assay kit where detection of mGluR binding in the presence

and absence of a test compound is performed. This example shows the integral role of detection in the method of selecting a protein that interferes with binding of a synaptic activation protein with a cellular binding protein. As the subject matter of claims 18 and 19 is disclosed in the specification as claimed, withdrawal of the rejection is respectfully requested.

Additionally, claims 16 and 20-23 are rejected as allegedly disclosing assay limitations that are not generally disclosed with respect to any binding protein to which the synaptic activation protein binds. It is respectfully submitted that the particular cellular binding proteins utilized in the examples of the application are merely exemplary and are not meant to be limiting to the subject matter of the application. For example, see page 13, lines 8-9, where it is stated that "*[a]s an example*...the rat Homer protein binds to two sub-types of metabotropic glutamate receptor (mGluR) found in the central nervous system - mGluR1α and mGluR5" (emphasis added). Not only does the specification set these cellular binding proteins forth as merely exemplary, the specification also states that other synaptic activation proteins will bind other cellular binding proteins. Further, the specification provides methods by which additional central nervous system binding partners may be identified. See, for example, pages 13-15 regarding identification of binding proteins and pages 15-17 regarding characterization of those binding partners. Therefore, it is respectfully submitted that it would have been clear to one of skill in the art that the assay limitations of claims 16 and 20-23 were directed generally to identification of a compound that interferes with binding of a synaptic activation protein to a cellular binding protein and that, if necessary, a binding partner for a synaptic activation protein could first be identified, using the disclosed methods. Therefore, it is respectfully submitted that, as drafted, claims 16 and 20-23 meet the written description requirement of 35 U.S.C. §112, first paragraph. Accordingly, withdrawal of the rejection is requested.

Applicants respectfully traverse the rejection of claims 10-11 and 13-23 under 35 U.S.C. § 112, first paragraph, as allegedly non-enabled because the body of claim 10 does not contain

steps that would establish that a test compound, once selected by the method of the claim would act in a similar manner in the central nervous system (*in vivo*).

The Examiner's attention is respectfully drawn to amended claim 10 above. By the present amendment, claim 10 has been amended to remove the language "in the mammalian central nervous system." The amended language of claim 10 is clearly directed to a screening assay, for detecting compounds that interfere with or modulate binding of a synaptic activation protein to a cellular binding protein. The process is not limited to an *in vivo* interference or modulation. The claim, as amended, is supported by the "screening assays" section on page 18 of the specification. This section of the specification also sets forth that compounds identified by such a screening assay may then be selected for drug development. These drugs may potentially be used in the treatment of epilepsy, abnormal brain development, neural injury, trauma and certain chemical addictions. However, such a use of the identified compounds is not part of claim 10. Claim 10 is directed to screening assays.

As such, one of skill in the art would have been able to practice the present invention, as the amended claims specify screening for a compound that interferes with or modulates binding of a synaptic activation protein to a cellular binding protein, and such a claim is fully supported by the specification. Therefore, claim 10, and claims 11 and 13-23, dependent from claim 10, meet the enablement requirement of 35 U.S.C. §112, first paragraph. Accordingly, withdrawal of the rejection is requested.

Applicants respectfully traverse the rejection of claim 14 under 35 U.S.C. §112, second paragraph as allegedly indefinite for failing to point out and distinctly claim the subject matter of the invention. It is alleged that claim 14 appears to be directed to the same subject matter as claim 13. Applicants respectfully disagree. Claim 14 encompasses a smaller amount of subject matter than claim 13. In order to clarify that claim 14 is a smaller subset of the mGluRs claimed in claim 13, and in order to advance prosecution of the subject application, the dependency of claim 14 has been changed, such that it now depends directly from claim 13.

Additionally, claim 15 has been rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite for recitation of the term "a Homer protein." The Examiner's attention is respectfully drawn to the amended language of claim 15. By the amendment, it has been clarified that the subject matter of claim 15 recites the method of claim 10, where the synaptic activation protein has 100% identity to SEQ ID NO: 2, where the protein is Homer. Support for this clarification may be found in the specification at, for example, page 2, line 34, where Homer is defined as "a rat protein, termed 'Homer' (SEQ ID NO: 2)."

Therefore, claims 14 and 15 meet the definiteness requirement of 35 U.S.C. §112, second paragraph. Accordingly, the withdrawal of the rejection is requested.

CONCLUSION

In summary, for the reasons set forth herein, Applicants maintain that claims 10, 11 and 13-23 clearly and patentably define the invention, respectfully request that the Examiner reconsider the various grounds set forth in the Office Action, and respectfully request the allowance of the claims which are now pending.

If the Examiner would like to discuss any of the issues raised in the Office Action, Applicants' representative can be reached at (858) 677-1456. Please charge any additional fees, or make any credits, to Deposit Account No. 50-1355.

Respectfully submitted,

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